

Claims:

1. A DNzyme which specifically cleaves RelA(p65) mRNA,  
the DNzyme comprising

- 5 (i) a catalytic domain which cleaves mRNA at a  
purine:pyrimidine cleavage site;  
(ii) a first binding domain contiguous with the 5' end  
of the catalytic domain; and  
(iii) a second binding domain contiguous with the 3' end  
10 of the catalytic domain,

wherein the binding domains are sufficiently  
complementary to the two regions immediately flanking a  
purine:pyrimidine cleavage site within the region of  
RelA(p65) mRNA corresponding to nucleotides 1 to 1767 as  
15 shown in SEQ ID NO:1, such that the DNzyme cleaves the  
RelA(p65) mRNA.

2. A DNzyme as claimed in claim 1 wherein each binding  
domain is nine or more nucleotides in length.

3. A DNzyme as claimed in claim 1 or claim 2 in which the  
catalytic domain has the nucleotide sequence GGCTAGCTACAACGA  
(SEQ ID NO: 2).

4. A DNzyme as claimed in any one of claims 1 to 3 in  
which the cleavage site corresponds to a site selected from  
the group consisting of:

- (i) the AT site at nucleotides 80-81;  
(ii) the GT site at nucleotides 91-92;  
30 (iii) the GT site at nucleotides 140-141;  
(iv) the AT site at nucleotides 149-150;  
(v) the AT site at nucleotides 215-216;  
(vi) the AT site at nucleotides 237-238;

(vii) the AT site at nucleotides 260-261;  
 (viii) the GT site at nucleotides 350-351;  
 (ix) the GT site at nucleotides 438-439;  
 (x) the AT site at nucleotides 479-480;  
 5 (xi) the GT site at nucleotides 525-526;  
 (xii) the GT site at nucleotides 572-572;  
 (xiii) the AT site at nucleotides 583-584;  
 (xiv) the GT site at nucleotides 726-727;  
 (xv) the GT site at nucleotides 734-735;  
 10 (xvi) the AT site at nucleotides 749-750;  
 (xvii) the AT site at nucleotides 807-808;  
 (xviii) the GT site at nucleotides 830-831;  
 (xix) the AT site at nucleotides 951-952;  
 (xx) the GT site at nucleotides 963-964;  
 15 (xxi) the AT site at nucleotides 1070-1071;  
 (xxii) the GT site at nucleotides 1076-1077;  
 (xxiii) the GT site at nucleotides 1100-1101;  
 (xxiv) the AT site at nucleotides 1125-1126;  
 (xxv) the AT site at nucleotides 1175-1176;  
 20 (xxvi) the GT site at nucleotides 1235-1236;  
 (xxvii) the AT site at nucleotides 1279-1280;  
 (xxviii) the GT site at nucleotides 1307-1308;  
 (xxix) the GT site at nucleotides 1313-1314;  
 (xxx) the GT site at nucleotides 1387-1388;  
 25 (xxxi) the AT site at nucleotides 1416-1417;  
 (xxxii) the GT site at nucleotides 1484-1485;  
 (xxxiii) the GT site at nucleotides 1529-1530;  
 (xxxiv) the AT site at nucleotides 1553-1554; and  
 (xxxv) the AT site at nucleotides 1697-1698.

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5. A DNAzyme as claimed in claim 4 in which the cleavage site corresponds to the GT site at nucleotides 91-92.

6. A DNzyme as claimed in claim 1 which has a sequence selected from the group consisting of:

5' GTTCGTCCAGGCTAGCTACAACGAGGCCGGGGT 3' (SEQ ID NO:3);  
5' GAGGGGGAAGGCTAGCTACAACGAAGTTCGTCC 3' (SEQ ID NO:4);  
5 5' TGATCTCCAGGCTAGCTACAACGAATAGGGGCC 3' (SEQ ID NO:5);  
5' GCTGCTCAAGGCTAGCTACAACGAGATCTCCAC 3' (SEQ ID NO:6);  
5' CGCCTGGGAGGCTAGCTACAACGAGCTGCCCCG 3' (SEQ ID NO:7);  
5' TTGGTGGTAGGCTAGCTACAACGACTGTGCTCC 3' (SEQ ID NO:8);  
5' TGATCTTGAGGCTAGCTACAACGAGGTGGGGTG 3' (SEQ ID NO:9);  
10 5' CCTTTCCTAGGCTAGCTACAACGAAAGCTCGTG 3' (SEQ ID NO:10);  
5' TTCTTCACAGGCTAGCTACAACGAACTGGATTC 3' (SEQ ID NO:11);  
5' TGGTCTGGAGGCTAGCTACAACGAGCGCTGACT 3' (SEQ ID NO:12);  
5' TAGTCCCCAGGCTAGCTACAACGAGCTGCTCTT 3' (SEQ ID NO:13);  
5' GGTCCCCGAGGCTAGCTACAACGATGTCACCTG 3' (SEQ ID NO:14);  
15 5' CCTGCCTGAGGCTAGCTACAACGAGGGTCCCGC 3' (SEQ ID NO:15);  
5' ACCTTGTCAGGCTAGCTACAACGAACAGTAGGA 3' (SEQ ID NO:16);  
5' CTTTCTGCAGGCTAGCTACAACGACTTGTCACA 3' (SEQ ID NO:17);  
5' ACACCTCAAGGCTAGCTACAACGAGTCCTCTTT 3' (SEQ ID NO:18);  
5' CGGTGCACAGGCTAGCTACAACGACAGCTTGCG 3' (SEQ ID NO:19);  
20 5' TCCGGAACAGGCTAGCTACAACGAAATGGCCAC 3' (SEQ ID NO:20);  
5' TCGTCTGTAGGCTAGCTACAACGACTGGCAGGT 3' (SEQ ID NO:21);  
5' ATCCGGTGAGGCTAGCTACAACGAGATCGTCTG 3' (SEQ ID NO:22);  
5' GCACAGCAAGGCTAGCTACAACGAGCGTCGAGG 3' (SEQ ID NO:23);  
5' GGGAAGGCAGGCTAGCTACAACGAAGCAATGCG 3' (SEQ ID NO:24);  
25 5' GCTTGGGGAGGCTAGCTACAACGAAGAAGCTGA 3' (SEQ ID NO:25);  
5' GTAAAGGGAGGCTAGCTACAACGAAGGGCTGGG 3' (SEQ ID NO:26);  
5' GAAACACCAGGCTAGCTACAACGAGGTGGGAAA 3' (SEQ ID NO:27);  
5' GGGGCAGGAGGCTAGCTACAACGATTGGGGAGG 3' (SEQ ID NO:28);  
5' CAGAGCTGAGGCTAGCTACAACGAACCATGGCT 3' (SEQ ID NO:29);  
30 5' GGA CTGGGAGGCTAGCTACAACGAAGGGCTGG 3' (SEQ ID NO:30);  
5' GGGCTAGGAGGCTAGCTACAACGATGGGACAGG 3' (SEQ ID NO:31);  
5' GGCCTCTGAGGCTAGCTACAACGAAGCGTTCCT 3' (SEQ ID NO:32);  
5' TCTTCATCAGGCTAGCTACAACGACAACTGCA 3' (SEQ ID NO:33);

5' AGTTGTCGAGGCTAGCTACAACGAGGATGCCAG 3' (SEQ ID NO:34);

5' GGGGGGCCAGGCTAGCTACAACGAAGGTATGCC 3' (SEQ ID NO:35);

5' CCATCAGCAGGCTAGCTACAACGAGGGCTCAGT 3' (SEQ ID NO:36);

and

5 5' AGAAGTCCAGGCTAGCTACAACGAGTCCGCAAT 3' (SEQ ID NO:37).

7. A DNAzyme as claimed in claim 6 which has the sequence  
5' GAGGGGGAAGGCTAGCTACAACGAAGTTCGTCC 3'.

10 8. A DNAzyme as claimed in any one of claims 1 to 7,  
wherein the 3'-end nucleotide residue is inverted in the  
binding domain contiguous with the 3' end of the catalytic  
domain.

15 9. A pharmaceutical composition comprising a DNAzyme  
according to any one of claims 1 to 8 and a pharmaceutically  
acceptable carrier.

20 10. A method of inhibiting NF- $\kappa$ B activity in a cell which  
method comprises introducing into the cell a DNAzyme of any  
one of claims 1 to 8.

11. A method of inhibiting NF- $\kappa$ B activity in a subject  
25 which method comprises administering to the subject a  
pharmaceutical composition of claim 9.

12. A method of treating an inflammatory disease in a  
subject which method comprises administering to the subject  
30 a therapeutically effective dose of a pharmaceutical  
composition of claim 9.

13. A method as claimed in claim 12, wherein the inflammatory disease is selected from the group consisting of inflammatory arthritis, asthma, inflammatory bowel disease, septic shock and vasculitis.

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14. A method as claimed in claim 13, wherein the inflammatory arthritis is selected from the group consisting of rheumatoid arthritis, osteoarthritis and seronegative arthritis.

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15. A method of treating atherosclerosis in a subject which method comprises administering to the subject a therapeutically effective dose of a pharmaceutical composition of claim 9.

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16. A method of treating cancer or leukaemia in a subject which comprises administering to the subject a therapeutically effective dose of a pharmaceutical composition of claim 9.

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17. A method as claimed in any one of claims 10 to 15, wherein the method is performed *in vivo*.

18. A method as claimed in any one of claims 10 to 15, wherein the method is performed *ex vivo*.

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